CLAIMS:

1. A method of staining targeted chromosomal material based upon nucleic acid sequence employing high complexity nucleic acid probes wherein said targeted chromosomal material is in the vicinity of a suspected genetic rearrangement associated with the retinoblastoma gene, chromosome 3 and/or chromosome 17 in humans.

2. A method according to Claim 1 wherein the targeted chromosomal material is one or more metaphase and/or interphase chromosomes, or one or more regions thereof.

3. A method according to Claim 2 wherein the chromosomal material is of fetal cells.

4. A method according to Claim 3 wherein the fetal cells have been separated from maternal blood.

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5. A method according to Claim 1 wherein said nucleic acid probes comprise heterogeneous mixtures of labeled nucleic acid fragments, wherein a substantial fraction of the sequences of the labeled nucleic acid fragments are substantially complementary to sites on chromosomal material that are targeted and are substantially free of nucleic acid sequences having hybridization capacity to sites on chromosomal material that is not targeted.

6. A method according to Claim 1 wherein the genetic rearrangement is selected from the group consisting of translocations, inversions, insertions, amplifications and deletions.

7. A method according to Claim 6 wherein the genetic rearrangement is selected from the group consisting of amplifications, deletions and translocations.

8. A method according to Claim 7 wherein the genetic rearrangement is associated with cancer.

9. A method according to Claim 8 wherein the genetic rearrangement is characteristic of retinoblastoma.

10. A method according to Claim 9 wherein the genetic rearrangement is a deletion.

11. A method according to Claim 8 wherein the genetic rearrangement is associated with chromosome 3.

12. A method according to Claim 11 wherein said nucleic acid probes are homologous to nucleic acid sequences in the p region of chromosome 3.

13. A method according to Claim 11 wherein said nucleic acid probes are homologous to nucleic acid sequences in the q region of chromosome 3.

14. A method according to Claim 1 wherein one component of the high complexity nucleic acid probe is targeted to paracentromeric-specific nucleic acid sequences.

15. A method according to Claim 14 wherein said paracentromeric-specific nucleic acid sequences are specific to chromosomes 3, 17, 13 and/or 21.

16. A method according to Claim 15 wherein the suspected genetic rearrangement is associated with the retinoblastoma gene and the para-centromeric-specific nucleic acid sequences are specific to chromosomes 13 and 21.

17. A method according to Claim 15 wherein the suspected genetic rearrangement is associated with chromosome 3 and the paracentromeric-specific nucleic acid sequences are specific for chromosome 3.

18. A method according to Claim 15 wherein the suspected genetic rearrangement is associated with chromosome 17 and the paracentromeric-specific nucleic acid sequences are specific for chromosome 17.

19. A method according to Claim 17 wherein another component of the high complexity nucleic acid probe is targeted to the 3p region and/or the 3q region of chromosome 3.

20. A method according to Claim 16 wherein another component of the high complexity nucleic acid probe is targeted to sequences within the retinoblastoma gene.

21. A method according to Claim 20 wherein these sequences are within different subregions of the retinoblastoma gene.

22. High complexity nucleic acid probes for the detection of genetic rearrangements associated with the retinoblastoma gene, chromosome 3, and/or chromosome 17 in humans.

23. High complexity nucleic acid probves according to Claim 22 wherein the complexity is greater than 50,000 bases.

24. High complexity nucleic acid probes according to Claim 22 wherein the genetic rearrangements are selected from the group consisting of translocations, inversions, insertions, amplifications and deletions.

25. High complexity nucleic acid probes according to Claim 24 wherein said genetic rearrangements are selected from the group consisting of translocations, deletions and amplifications.

26. A method of detecting genetic rearrangements associated with the retinoblastoma gene, chromosome 3, and/or chromosome 17 in humans comprising the steps of:

a. hybridizing the probes of Claim 22 to targeted chromosomal material in the vicinity of a suspected genetic rearrangement;

b. observing and/or measuring the proximity of and/or other characteristics of the signals from said probes; and

c. determining from said observations and/or measurements obtained in step b) whether a genetic rearrangement has occurred.

27. A method according to Claim 26 wherein the chromosomal material is in interphase.

28. A method according to Claim 26 wherein the suspected genetic rearrangement is diagnostic or prognostic of cancer.

29. A method of staining chromosomes from different cells with high complexity probes to determine differences between the chromosomes of different cells.

30. A method according to Claim 29 wherein those cells are from a solid tumor from a human patient.

31. A method according to Claim 30 wherein the solid tumor is a breast cancer and wherein the high complexity probes are targeted to sequences within the retinoblastoma gene.

32. A method according to Claim 29 wherein differences of the karyotypes between normal and malignant cells and differences between malignant cells are determined.

33. A method according to Claim 32 wherein staining patterns produced therefrom are used to distinguish normal and malignant cells for purposes of diagnosis, prognosis and/or determining the effectiveness of therapy.

34 A method of staining targeted chromosomal material in the vicinity of a suspected genetic rearrangement with high complexity nucleic acid probes according to Claim 22 wherein the probe nucleic acid sequences prior to hybridization to the targeted chromosomal material are broken into fragments of from about 200 bases to about 600 bases.

35. Chromosome-specific staining reagent comprising a heterogeneous mixture of labeled nucleic acid fragments, wherein the labeled nucleic acid fragments are complementary to sites on targeted chromosomal material in the vicinity of suspected genetic rearrangements associated with the retinoblastoma gene, chromosome 3, and/or chromosome 17 in humans,

and are substantially free of nucleic acid sequences having hybridization capacity to sites on non-targeted chromosomal material.

36. The chromosome-specific staining reagent of Claim 35 wherein said labeled nucleic acid fragments are single-stranded.

37. The chromosome-specific staining reagent of Claim 35 wherein said nucleic acid fragments are labeled with radioactive, enzymatic, immunoreactive, fluorochromes and/or affinity detectable reagents.

38. The chromosome-specific staining reagent of Claim 35 wherein said fragments are biotinylated, modified with N-acetoxy-N-2-acetylaminofluorene, modified with fluorescein isothiocyanate, modified with mercury/TNP ligand, sulfonated, digoxigenenated, or contain T-T dimers.

39. A chromosome-specific staining reagent that provides staining patterns indicative of a genetic rearrangement associated with the retinoblastoma gene, chromosome 3, and/or chromosome 17 in humans, produced by the process of:

isolating chromosome-specific DNA;

amplifying pieces of the isolated chromosome-specific DNA;

disabling the hybridization capacity of and/or removing shared repetitive sequences contained in the amplified pieces of the isolated DNA to form a collection of nucleic acid fragments which hybridize predominantly to

targeted chromosomal DNA in the vicinity of a suspected genetic rearrangement; and

labeling the nucleic acid fragments of the collection to form a heterogeneous mixture of nucleic acid fragments.

40. A chromosome-specific staining reagent according to Claim 39 wherein said step of amplifying said pieces of isolated DNA is performed by cloning.

41. A chromosome-specific staining reagent according to Claim 39 wherein said step of amplifying said pieces of isolated DNA is performed by using the polymerase chain reaction (PCR).

42. A method of staining targeted chromosomal material with high complexity nucleic acid probes according to Claim 22 to produce staining patterns indicative of genetic rearrangements comprising the steps of:

providing a heterogeneous mixture of labeled nucleic acid fragements, wherein substantial proportions of the labeled nucleic acid fragments in the heterogeneous mixture have base sequences substantially complementary to the targeted chromosomal material which is in the vicinity of a suspected genetic rearrangement;

reacting the heterogeneous mixture with the targeted chromosomal DNA by in situ hybridization; and

observing and/or measuring the proximity of and/or other characteristics of signals of said staining patterns to determine whether a genetic rearrangement has occurred.

43. Test kits comprising the probes of Claim 22.

44. High complexity nucleic acid probes according to Claim 22 for use in biological dosimetry.

45. High complexity nucleic acid probes according to Claim 22 for use in prenatal testing.

46. A method of detecting a deletion in a specific portion of a gene comprising the use of high complexity nucleic acid probes for differential staining of subregions within the gene.

47. A method according to Claim 46 wherein said gene is the retinoblastoma gene.